Application No. 10/019,816
Filed: March 27, 2002
TC Art Unit: 1643
Confirmation No.: 9944

REMARKS

The pending claims have been rejected under 35 USC § 112 for lack of enablement. The rejection is respectfully traversed in light of the remarks given below and reconsideration is requested.

In particular, claims 220, 242-243, 247, 249, 252-254, 264-265, 270-271 and 273-274 are newly cancelled. Claims 275 to 282 are added. Claims 217, 218-219, 221, 244-245 and 266-268 are amended herein. Applicant's amendment or cancellation of certain rejected claims is not to be construed as an admission that the Examiner's rejections were proper. The Applicant continues to believe that the rejected claims are described in and enabled by the specification, as previously argued. The rejected claims have been amended or cancelled for the sole purpose of advancing the case to allowance. The Applicant reserves the right to file a continuing application to continue the prosecution of the rejected claims.

The independent claims as amended are now directed to the use of a polypeptide comprising a cytoplasmic fragment of a β integrin subunit providing a binding domain of the subunit for a MAP kinase, or the polypeptide having a modified amino acid sequence compared to the binding domain. The binding domain is defined as incorporating an amino acid linker sequence that links opposite end regions of the binding domain together and which is non-essential to the binding of the MAP kinase. The modified amino acid sequence is further defined as having at least 50% overall sequence identity with the binding domain and sufficient sequence homology with both the end regions of the binding domain to bind to the MAP kinase. The independent claims also now define the MAP

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kinase as being ERK2 and the β integrin subunit being selected from the group consisting of β3, β5 and β6.

Support for the amendments is found throughout the specification such as, for example, page 25, lines 2 to 9; page 87, lines 3 to 11; page 25, line 11 to page 27, line 11; page 49, line 16 to page 50, line 20; and page 24, line 24 to page 25, line 2. With regard to the length of the polypeptide defined in new claims 275-276 and 279-280, it is further noted that the above disclosure bridging pages 49 and 50 states that a polypeptide useful in the present invention may have a length of "less than about 40 amino acids. Preferably, the length will be from between about 5 to 30 amino acids, and more preferably from between about 5 amino acids and about 25 amino acids." The specification at the cited place goes on to further exemplify the peptide RSKAKWQTGTNPLYR and the peptide RSKAKNPLYR, which are 15 amino acids and 10 amino acids in length, respectively. Accordingly, the passage clearly specifies length "ranges" of polypeptides and encompasses each and every polypeptide length within the limits of the defined range(s). Moreover, page 27, lines 3 to 9, exemplifies the 20 mer polypeptide RSKAKWQTGTNPLYRGSTST incorporating the binding domain of β6 for ERK2.

Applicant submits that amendment of the claims to refer specifically to ERK2 and to a β integrin subunit selected from β3, β5 and β6 overcome those objections raised on the basis of the assertion the specification does not reasonably provide enablement for the disruption of the binding of MAP kinases to β integrin subunits beyond ERK2 and β3, β5 and β6.

With regard to the Examiner's concern with the terminology "modified amino acid sequence," it is submitted that the claims as

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amended are specifically limited to "technical features" of the sequence in terms of its overall amino acid homology with the binding domain and sequence identity with the end regions of the binding domain of the β integrin subunit. That is, only polypeptides having an amino acid sequence with sequence identity to the end regions of the binding domain to a level sufficient for binding of the MAP kinase to the β integrin subunit are encompassed. In this regard, the Examiner's attention is again drawn to page 45, line 3 to page 46, line 12 of the specification to the effect that the localization and characterization of the binding domain of a β integrin subunit for a MAP kinase permits the design of alternative forms of the binding domain. Hence, with knowledge of the binding domain of a β integrin subunit as taught by the present application, amino acid changes can be made such that while the amino acid sequence is modified, the capacity to bind to the MAP kinase is retained as specifically provided for by the specification (see page 25, line 10 to page 27, line 11). The specification clearly provides for the provision of modified amino acid sequences that while differing from the amino acid sequence of the binding domain, nevertheless retain their capacity to bind to the MAP kinase. Indeed, and as indicated above, the specification specifically exemplifies the provision of a 10 mer peptide (RSKAKNPLYR) which retains the ability to bind to β6 following deletion of the linker sequence WQTGT (see page 87, lines 6 to 9).

Accordingly, those of ordinary skill in the art would be led to provide such other sequences in light of the instant invention without undue experimentation. It is further submitted that the modification of known amino acid sequences by conservative amino acid changes is well within the scope of one of ordinary skill and

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constitutes mere routine experimentation which the skilled addressee would be able to readily undertake on the basis of the teachings and methodology set out present application. It is also submitted it is not incumbent on an Applicant to disclose all possible alternatives of a claimed invention. The specification provides a concrete teaching of the provision of polypeptides with modified amino acid sequences compared to the binding domain of the corresponding integrin β subunit, and the provision of further such polypeptides within the scope of the claims as amended is merely the application of ordinary skill of the skilled addressee not requiring inventive input.

With regard to the Examiner's assertion that the specification does not teach a means for the delivery of the polypeptides of present interest to the site of action and efficacious uptake by tumor cells to obtain inhibition of the cancer cells *in vivo*, the Examiner's attention is directed to page 54, line 19 to page 55 which teach use of facilitator moieties such as carrier peptides to deliver the active polypeptide across the outer cell membrane of the cancer cells. Attention is additionally drawn to page 56, line 15 to page 59, line 13 describing ways in which the polypeptides may be formulated and administered for treatment of the cancer.

In this regard, inventor Michael Valentine Agrez has conducted *in vivo* studies and has shown that different peptides encompassed by the instant method claims and disclosed in the specification can be formulated in normal saline or standard buffer (DMEM) and administered by a number of different routes (e.g., intratumorally, subcutaneously, intraperitoneally) to nude mice to provide efficacious treatment against a number of cancers including colon cancer xenografts and prostate cancer xenografts. Accordingly, it

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is further submitted that one of ordinary skill can readily put methods of the invention into effect on the basis of the teachings provided by the instant specification with routine trial and experimentation without inventive input. A statutory declaration by Dr. Agrez attesting to the efficacy of the *in vivo* administration of polypeptides described in the instant specification is currently being prepared and will submitted to the Examiner shortly.

With regard to the objection raised by the Examiner relating to the use of the term "prophylaxis" in the method of treatment claims 247 and 266, the Applicant has cancelled claim 247 (thus rendering that rejection moot) and amended claim 266 to remove "prophylaxis" from the preamble and to include, prior to the "administering" step, the step of "providing a mammalian patient suffering from or believed to be at risk of suffering from cancer." Applicant submits that these amendments do not change the scope of claim 266 and the claims dependent thereon as the term "prophylaxis" was intended to have its ordinary definition of relating to a measure designed to preserve health and prevent the spread of disease, as indicated in the specification.

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The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

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